In re: Herrington et al. Serial No.: 10/081,563

Filed: February 22, 2002

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In the Specification:

Please replace the title at page 1, and all following occurrences of the title, with the following:

GENETIC POLYMORPHISMS OF ESTROGEN RECEPTOR ALPHA ASSOCIATED WITH FAVORABLE HOL—CHOLESTEROL RESPONSE TO HORMONE REPLACEMENT THERAPY

Please replace paragraph [0010] with the following amended paragraph:

[0010] A first aspect of the present invention is, accordingly, a method of screening a subject for increased likelihood of having a favorable response to estrogen replacement therapy[[.]], particularly with respect to cardiovascular health (e.g., improved future cardiovascular health as compared to that found in the same patient without estrogen replacement therapy; a decreased probability of [[],]] heart disease (e.g., a decreased, heart disease (i.e., high density lipoprotein (HDL) level)). The method comprises detecting the presence of at least one estrogen receptor alpha polymorphism in the subject, the presence of the estrogen receptor alpha polymorphism indicating the subject is more likely to have a favorable response to estrogen replacement therapy.

Please replace paragraph [0012] with the following amended paragraph:

[0012] A second aspect of the present invention is a method for beneficially affecting cardiovascular health, decreasing the risk of heart disease, and/or increasing HDL levels in a subject (e.g. beneficially altering the LDL/HDL ratio), the method comprising: (a) determining the presence of at least one estrogen receptor alpha polymorphism in said subject; and then, if said estrogen receptor alpha polymorphism is present, (b) administering estrogen replacement therapy to said subject in an amount effective to beneficially affect cardiovascular health, decrease the risk of heart disease, and/orinerease or increase HDL levels in said subject. Polymorphisms of interest are as discussed aboveabove.

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Please replace paragraph [0032] with the following amended paragraph:

[0032] Determining the presence or absence of DNA containing a polymorphism of interest may be carried out with an oligonucleotide probe labelled with a suitable detectable group, or by means of an amplification reaction such as a polymerase chain reaction or ligase chain reaction (the product of which amplification reaction may then be detected with a labelled oligonucleotide probe or a number of other techniques). Further, the detecting step may include the step of detecting whether the subject is heterozygous or homozygous for the polymorphism of interest. Numerous different oligonucleotide probe assay formats are known which may be employed to carry out the present invention. See, e.g., U.S. Pat. No. 4,302,204 to Wahl et al.; U.S. Pat. No. 4,358,535 to Falkow et al.; U.S. Pat. No. 4,563,419 to Ranki et al.; and U.S. Pat. No. 4,994,373 to Stavrianopoulos et al. (applicants specifically intend that the disclosures of all U.S. Patent references cited herein be incorporated herein by reference).

Please replace paragraph [0043] with the following amended paragraph:

[0043] Estrogen replacement therapy may be carried out by any suitable means. All typically involve administering an active agent such as estrogen or an estrogen analog (typically a steroid that has estrogen activity) to the subject in an estrogen replacement therapy effective amount, which is generally commensurate with an amount effective to enhance HDL levels as discussed above. Any suitable route of administration may be employed, including, but not limited to, oral administration, aerosol administration to airway surfaces, intravenous injection, subcutaneous injection, intramuscular injection, transdermal administration (e.g., a patch), etc. Oral and transdermal formulations are currently preferred. Numerous estrogen replacement therapy preparations and protocols are known, including but not limited to those described in U.S. Patents Nos. 5,922,349; 5,897,539; 5,565,199; 5,468,736; 5,422,119; 5,288,717; and 5,023,084, the disclosures of all of which are incorporated by reference herein in their entirety. Other agents, such as progesterone (or progestin) in a hormone replacement therapy effective amount, may be administered along with the estrogen to provide a combination therapy, if

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desired (typically to reduce undesirable side-effects of estrogen monotherapy, as such estrogenic endometrial proliferation and corresponding risk of endometrial cancer).